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Desmoplastic Fibroma Arising in Fibrous Dysplasia

Chromosomal Analysis and Review of the Literature

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A desmoplastic fibroma of bone arose in the fibula of a 17-year-old boy with fibrous dysplasia. This may be the second case of this rare histopathologic association reported in the literature. Benign bone tumors have not previously been subjected to cytogenetic analysis. Analysis of this case revealed a primary abnormal clone trisomic for both chromosomes 3 and 5 and two subclones, one trisomic for chromosome 3 and one trisomic for chromosome 5. This case may also present the first description of nonrandom karyotypic abnormalities in a benign neoplasm of bone.

Fibrous dysplasia of bone was described by Jaffe[8] as a skeletal disorder in which fibroosseous tissue is produced in the cancellous portion of the bone. It is a common lesion and was classified by Lichtenstein and Jaffe[9] as a congenital or developmental anomaly due to a disturbance of the bone-forming mesenchyme. Benign entities arising in bone affected with fibrous dysplasia are almost nonexistent. West *et al.*[22] described the only distinct benign lesion, a desmoplastic fibroma of bone (DFB), known to arise in bone affected with fibrous dysplasia.

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Recently, several benign and malignant soft-tissue tumors have been shown to have characteristic chromosomal aberrations, which are important both diagnostically and in understanding the molecular pathogenesis of these neoplasms.[16] Few reports exist describing cytogenetic abnormalities in primary malignant bone tumors, and there are no reports of cytogenetic analysis of benign bone tumors. The authors report the second known case of a DFB arising in bone affected with fibrous dysplasia. A review of DFB arising in fibrous dysplasia and a chromosomal analysis of this tumor are presented.

CASE REPORT

A 17-year-old white boy presented with persistent left lateral knee pain. Four days prior to seeking medical attention, the patient had sustained a valgus-producing force to his left knee while playing football. A physical examination demonstrated no soft-tissue mass. Roentgenograms demonstrated a fusiform expansion of the proximal one third of the fibula with cortical thinning and a trabeculated appearance (Fig. 1).[13] Magnetic resonance imaging confirmed the absence of soft-tissue extension. An excisional biopsy of the proximal fibula was performed (Fig. 2).

The specimen consisted of a portion of fibula measuring 3.0 × 17.5 cm in greatest dimension. A 9-cm firm, white homogeneous lesion was present within the marrow of the midshaft of the specimen. Microscopically, there were areas of misshapen trabeculae interspersed with fibrous tissue

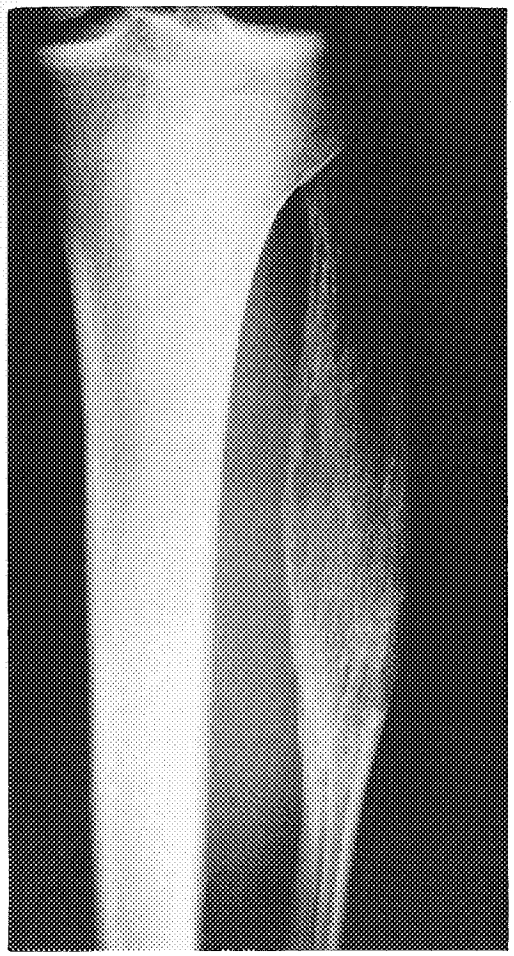

FIG. 1. A roentgenogram demonstrating the anteroposterior projection of a fusiform expansile lesion involving the proximal metaphyseal region of the left fibula in a 17-year-old boy.

(Fig. 3) and other areas dominated by small fibroblasts with intercellular material rich in collagen and lacking bony trabeculae (Fig. 4). A random mixture of these two lesions was seen (Fig. 5). Consultation with another physician at a cancer center confirmed the diagnosis of a DFB arising in fibrous dysplasia.[6] A portion of this specimen was studied cytogenetically.

MATERIALS AND METHODS

A 1-cm^3 specimen sample was obtained directly from surgery and placed into Roswell Park Memorial Institute 1640 media (Gibco, Grand Island, New York) supplemented with 20% fetal bovine serum and antibiotics. The specimen was disaggregated, and cultures were prepared using the technique described by Gibas *et al.*[3] The specimen was harvested following ten days of incubation. Twelve hours prior to the initiation of harvest, cells were exposed to colcemid (0.02 μg/ml), followed by centrifugation, removal of the supernatant, and incubation in hypotonic solution composed of 0.074 M KCl for 30 minutes. Subsequently, the cells were fixed three times with methanol/glacial acetic acid (3:1), and the cell suspension was dropped onto cold, wet slides and G-banded according to the method of Yunis.[24]

RESULTS

Twenty metaphase cells were analyzed. Of these, 11 cells were chromosomally normal. Of the remaining cells, three abnormal clones were detected: three cells were trisomic for chromosome 3, three trisomic for chromosome 5, and three trisomic for both chromosomes 3 and 5 (46,XY/47,XY,+3/47,XY,+5/48,XY,+3,+5). The abnormal clones trisomic for chromosomes 3 and 5 are most likely subclones derived from the primary abnormal clone trisomic for both chromosomes 3 and 5. Definition of the clones was difficult, however, because a few of the cells also contained several random abnormalities. A representative karyotype of one of the metaphase cells trisomic for chromosome 3 is presented in Figure 6.

DISCUSSION

Fibrous dysplasia is a common nonneoplastic fibroosseous lesion of bone. Harris *et al.*[4] and Reed[14] emphasized that it may represent a maturation defect of coarse fiber bone to lamellar bone. In a study of 69 cases, Schlumberger[17] demonstrated that the most common sites of skeletal involvement were the ribs, femur, tibia, maxilla, and calvarium.

Infrequently, malignancy may supervene in fibrous dysplasia of bone. Osteosarcoma,

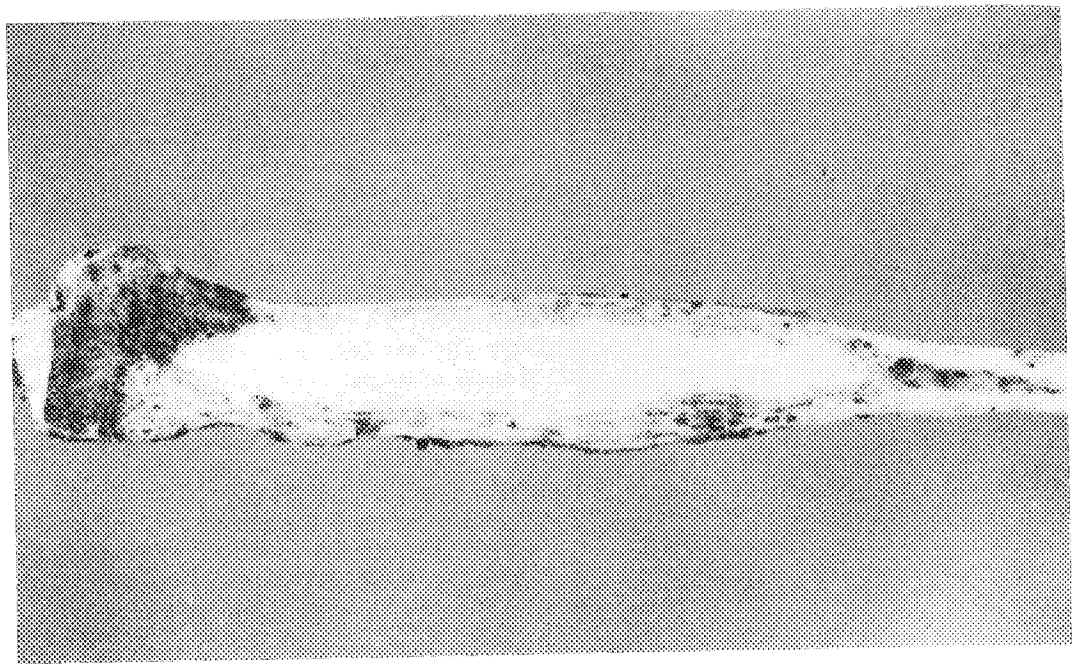

FIG. 2. The excisional biopsy of the proximal fibula demonstrating a white homogeneous lesion present within the medullary canal of the specimen. (Original magnification, ×25.)

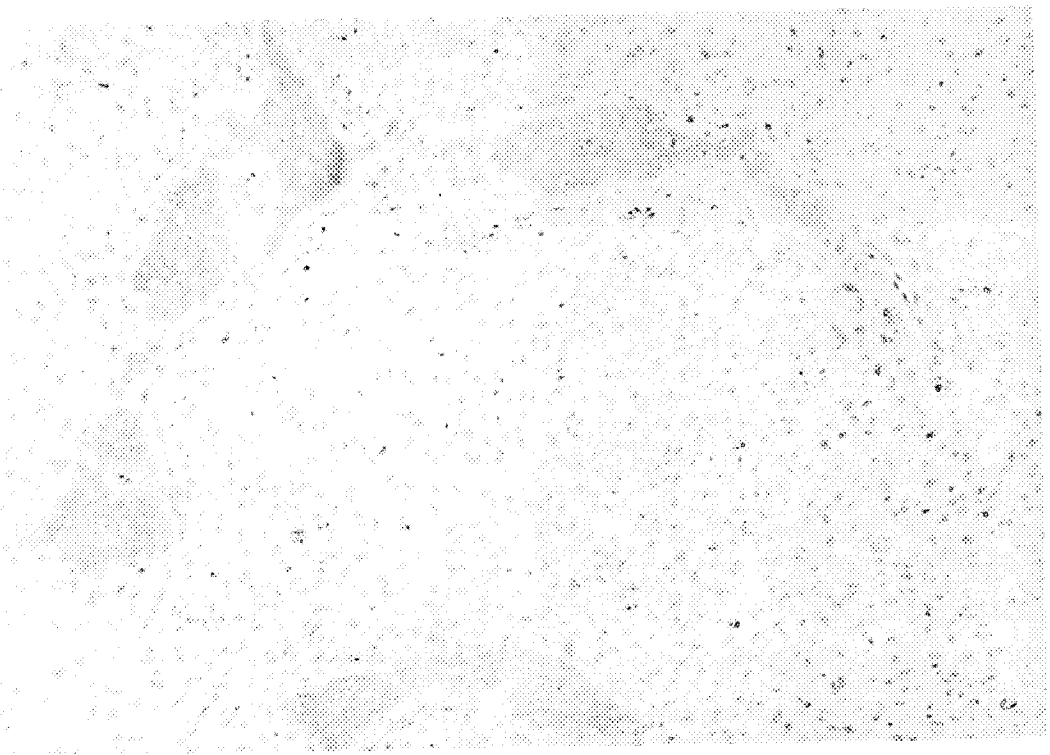

FIG. 3. Misshapen bony trabeculae with intervening cellular fibrous tissue characteristic of fibrous dysplasia. Osteoblastic rimming is not present. (Stain, hematoxylin and eosin; original magnification, ×150.)

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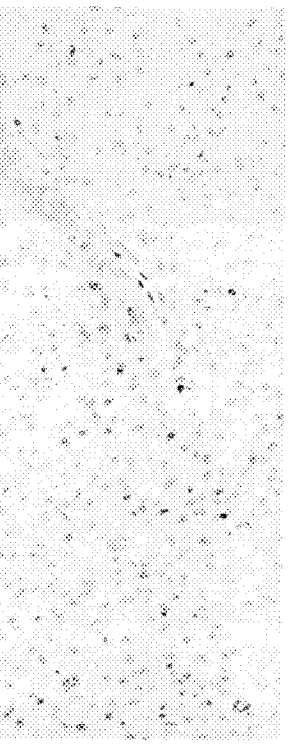

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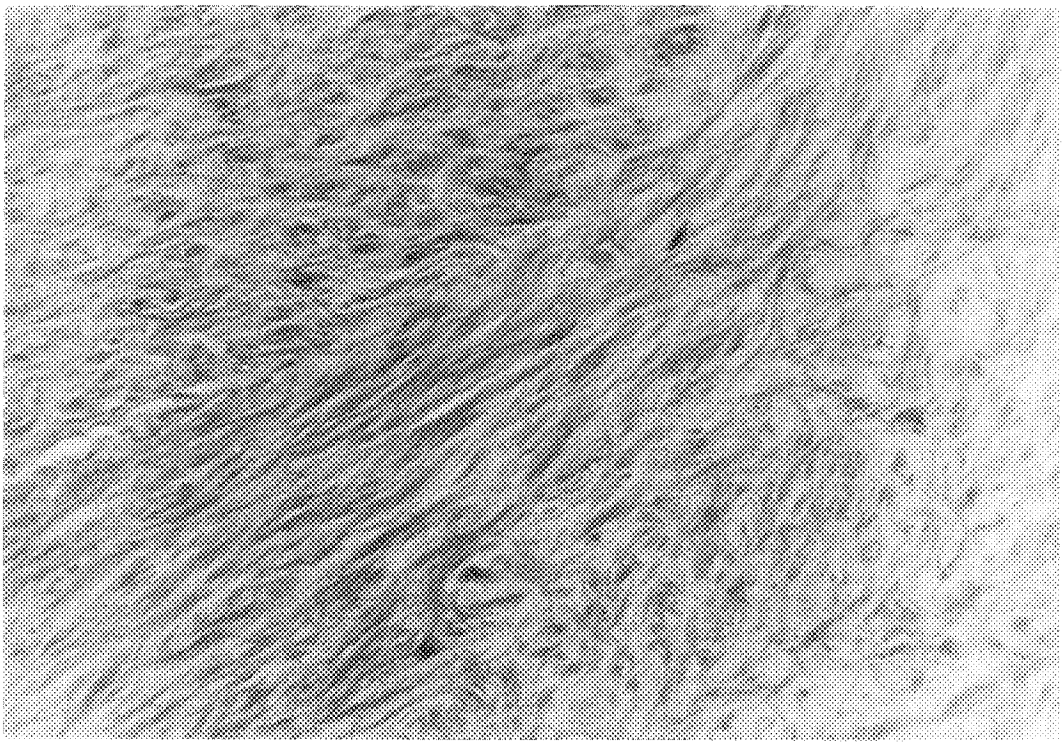

FIG. 4. Well-differentiated, slightly cellular fibrous tissue with thick hyalinized collagen fibers characteristic of desmoplastic fibroma. (Stain, hematoxylin and eosin; original magnification, ×220.)

fibrosarcoma, and chondrosarcoma are the most commonly reported associated sarcomas.[7] Association with other histologically distinct benign lesions is extremely rare. In the present case, the occurrence of a desmoplastic fibroma of the fibula in a 17-year-old boy was associated with monostotic fibrous dysplasia of the same bone. Only one other case with this association has been described.[22]

In both the present case and the previously reported case of DFB arising in fibrous dysplasia, the lesions occurred in symptomatic young adult males with roentgenographically evident, centrally destructive lesions of the bone. These lesions demonstrated increased uptake on the bone scan. In the present case, however, the lesion was localized to the medullary canal of the fibula as opposed to the previously reported patient in whom soft-tissue extension of a mass involving the pubis and ilium was present. Neither patient has had a history of other bone problems, endocrinologic abnormalities, or unusual pigmentation.

Since the mutational theory of cancer was formulated at the turn of this century, chromosomal changes have been implicated as the etiologic and/or pathogenetic factors in carcinogenesis. In the past few years, knowledge concerning chromosomal aberrations in mesenchymal tumors has increased. Several of these tumors, including Ewing's sarcoma, synovial sarcoma, and myxoid liposarcoma, have demonstrated specific cytogenetic abnormalities.[1,2,10,18,19,21,23] These

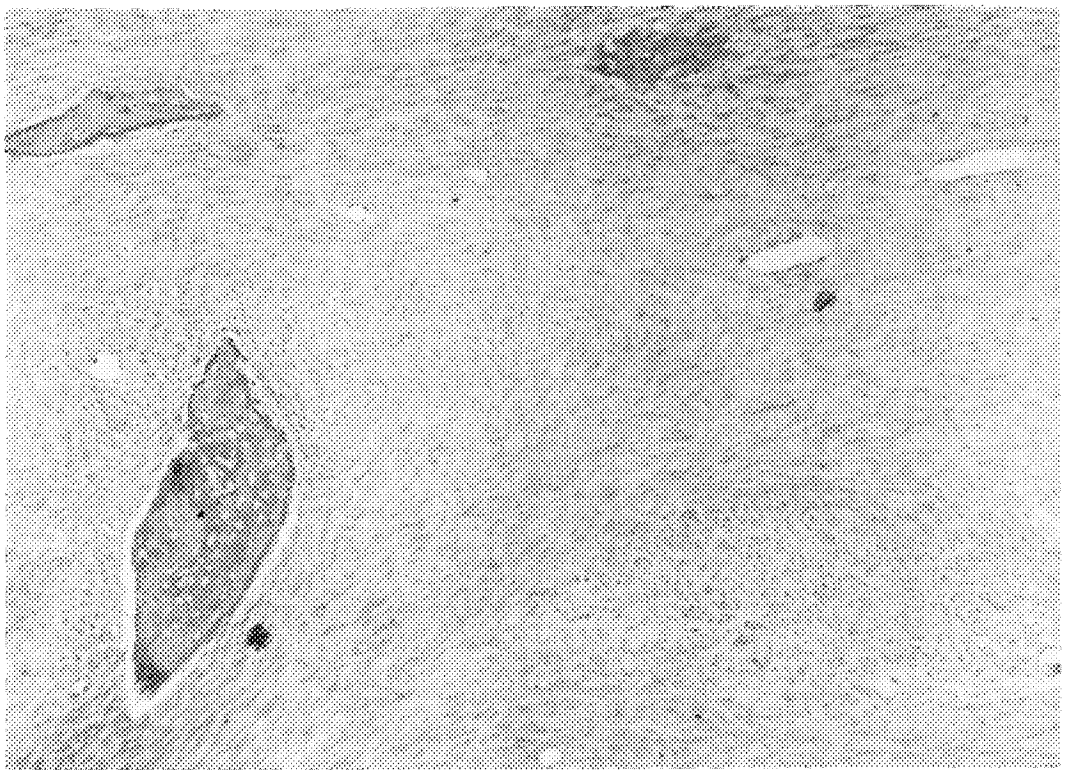

FIG. 5. A random mixture of the fibrous dysplasia (upper left corner) and the desmoplastic fibroma (lower right corner). (Stain, hematoxylin and eosin; original magnification, ×100.)

cytogenetic abnormalities have been useful in establishing a diagnosis when there is difficulty with conventional histologic approaches and in providing insight into the histogenesis of many of these tumors.

Cytogenetic studies of primary malignant bone tumors are few.[1,11,21,23] There are no reports of chromosome findings in primary benign bone tumors. Although the majority of tumors studied in the literature with specific chromosomal aberrations are malignant, several benign tumors have also demonstrated specific chromosomal changes. A documented example is the reciprocal translocation t(3;12)(q27-28;q13-14) in benign lipomas.[5,20] The presence of this specific translocation in lipoma but not in liposarcoma serves as an additional useful diagnostic tool because of the difficult overlapping morphologic features seen in lipoma versus well-differentiated liposarcoma.

Cytogenetic analysis of this DFB arising in fibrous dysplasia revealed a primary abnormal clone that was trisomic for chromosomes 3 and 5 in three of 20 cells analyzed. Furthermore, six additional cells appeared to have been derived from the primary clone; three were trisomic for chromosome 3 only, and the other three were trisomic for chromosome 5 only. These six cells most likely represent subclones. Although the above abnormalities were clonal, the variation from cell to cell was substantial, indicating several random abnormalities as well.

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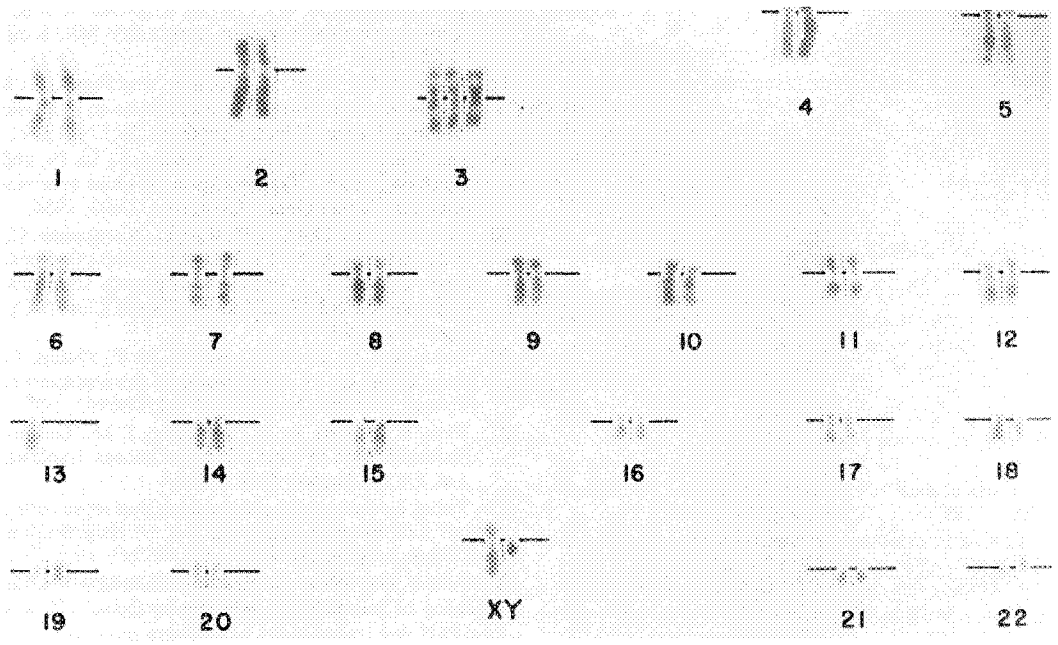

FIG. 6. Representative karyotype, trisomic for chromosome 3.

Benign tumors are not generally associated with clonal chromosome abnormalities. However, clonal chromosome abnormalities have been reported in association with lipomas, meningiomas, and colonic adenomas.[5,12,15,20,25] The authors have studied a chondromyxoid fibroma of bone that demonstrated both structural and numerical chromosomal aberrations. An identical numerical abnormality (trisomy 5) was shared by the DFB arising in fibrous dysplasia and the chondromyxoid fibroma of bone. Additional cases must be studied to determine the significance of these findings. The observation of a clonal abnormality in this DFB arising in fibrous dysplasia may represent another benign state associated with a specific chromosomal change. It is not known if malignancies will develop in individuals who have been identified as having a clonal chromosome abnormality in a histologically benign lesion.

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